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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/487,851	01/19/2000	Robert J. Levy	7600-20U1 (CHOP-0013)	3653

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/487,851	LEVY ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/29/03 & 11/10/03* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,5,16,17,31-34,36-38,65,67 and 68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,5,16,17,31-34,36-38,65,67 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The response and amendment filed 8/29/03 and the Declaration filed 11/10/03 are acknowledged. Claims 30, 35, 66, 69, and 70 have been canceled. Claims 4, 5, 16, 31, 34, 36, 65, and 67 have been amended. Claims 4, 5, 16, 17, 31-34, 36-38, 65, 67, and 68 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims and the Declaration will not be reiterated. The arguments in the 8/29/03 paper would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 5, 16, 17, 31-34, 36-38, 65, 67, and 68 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for alleviating *re-entrant artrial flutter* comprising locally delivering to myocardial cells a plasmid vector comprising a promoter operably linked with a nucleic acid encoding a defective HERG protein, does not reasonably provide enablement for alleviating any disease or any arrhythmias comprising locally delivering to myocardial cells any vector comprising a promoter operably linked with a nucleic acid encoding a defective HERG

protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In 8/29/03 amendment, in response to the previous rejection based on Bradley Nuss reference, applicants argue that the cause of the hyperexcitability is different in the case of Nuss compared to the instant reentrant artrial flutter, that Nuss et al aimed to treat a cardiac condition caused by abnormalities in repolarization, while the instant invention aims to treat a cardiac arrhythmia caused by tachyarrthmic conduction circuits, which are distinct and opposite causes of cardiac hyperexictability.

In response, these arguments further support the position of the Office that the claimed invention is based on the knowledge of the skilled in the art and the understanding of the etiology of reentrant artrial flutter, and that delivery of a defective HERG gene could not alleviate any disease, any arrhythmias, or any myocardial hyperexcitability caused disease. Evidently each disease has its own distinct etiology and pathophysiology, administering a defective HERG gene will not alleviate abnormalities of repolarization and EADs, and there is no evidence on the record that it will alleviate diseases other than reentrant artrial flutter.

With respect to the type of vectors used for alleviating re-entrant artrial flutter, as a general rule in the relevant art, the *in vivo* efficiency of various vectors infecting/transfecting various target cells is unpredictable, particularly when a therapeutic effect is required. *Orkin et al* teach that major difficulties for gene therapy include shortcomings in all current gene transfer vectors and an inadequate

understanding of the biological interaction of these vectors with the host. In view of such, specific, not general teaching is required with regard to how to use various vectors known in the art and how to control the *in vivo* condition such that a particular vector is able to transfect a significant amount of the target cells and expressing the heterologous gene at a significant level such that a therapeutically beneficial effect could be obtained. To this end, the specification teaches extensively a plasmid vector and using such together with other carrier substance such as liposome as illustrative embodiment for the local delivery of heterologous gene. The later submitted supporting data are also generated from the experiments conducted with a plasmid vector. Thus, the specification fails to provide sufficient guidance to support the full scope of the claims with regard to using any type of vectors.

Accordingly, for reasons of record and those set forth above, the instant specification fails to meet the enablement requirement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 5, 16, 17, 30-38, and 65-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the limitation "the cardiac cell" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Patent Examiner
Art Unit 1632

QL
November 13, 2003

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER